AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of all claims in the application.

Listing of Claims

1. (**Original**) A modified arrestin comprising an arrestin or a biologically active fragment of arrestin and a ubiquitin moiety or a biologically active fragment of ubiquitin, wherein the modified arrestin has an increased affinity for a GPCR, as compared to the affinity of a wild-type arrestin for a GPCR, and wherein increased affinity means that the arrestin remains associated with the GPCR and traffics with the GPCR into endosomes, and wherein the arrestin does not dissociate at or near the plasma membrane.

2. (**Original**) The modified arrestin of claim 1, wherein the ubiquitin is covalently linked to the arrestin.

3. (**Original**) The modified arrestin of claim 2, wherein the ubiquitin is linked to a Lysine.

4. (**Original**) The modified arrestin of claim 1, wherein the ubiquitin is susceptible to deubiquitination.

5. (**Original**) The modified arrestin of claim 1, wherein the ubiquitin is linked to the 5' or 3' end of arrestin.

6. (**Original**) The modified arrestin of claim 1, wherein the modified arrestin further comprises a label, and wherein the label is a radioisotope, an epitope tag, an affinity label, an enzyme, a fluorescent group, or a chemiluminescent group.

7. **(Currently Amended)** The modified arrestin of claim 1, wherein the modified arrestin comprises the amino acid sequence of ~~SEQ ID NO:1, SEQ ID NO: 2, or SEQ ID NO: 3~~ **SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6**.

8. **(Original)** A nucleic acid sequence encoding the modified arrestin of claim 1.

9. **(Currently Amended)** A nucleic acid comprising the nucleic acid sequence of ~~SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6~~ **SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5**.

10. **(Original)** A nucleic acid degenerate to the nucleic acid of claim 9.

11. **(Original)** A nucleic acid complementary to the nucleic acid of claim 9.

12. **(Original)** An expression vector comprising the nucleic acid sequence of claim 8 operably linked to an expression control sequence.

13. **(Original)** A host cell expressing one or more of the modified arrestin of claim 1.

14. **(Original)** A host cell comprising the expression vector of claim 12.

15. **(Original)** The host cell of claim 13, wherein the host cell further comprises a GPCR.

16. **(Original)** The host cell of claim 13, wherein the host cell is a mammalian, 15 bacterial, yeast, plant, insect, or animal cell.

17. **(Original)** The host cell of claim 13, wherein the cell is deposited on a substrate.

18. **(Original)** The modified arrestin of claim 1, wherein the modified arrestin comprises one or more ubiquitin molecules.

19. **(Original)** The modified arrestin of claim 18, wherein the modified arrestin comprises one or more chains of two or more ubiquitin molecules, wherein at least one of the ubiquitin molecules is attached to the arrestin.

20. **(Original)** The modified arrestin of claim 1, wherein the GPCR is a class A GPCR.

21. **(Original)** The modified arrestin of claim **1**, wherein the modified arrestin increases the internalization of the GPCR.

22. **(Currently Amended)** The modified arrestin of claim **1**, wherein the arrestin is a visual arrestin, a cone arrestin, ~~a (β-arrestin 1, a (β-arrestin 2,~~ **β-arrestin 1, a β-arrestin 2,** or any other naturally occurring or engineered variant of arrestin.

23. **(Original)** A substrate having deposited thereon a plurality of cells, wherein the cells express at least one modified arrestin.

24. **(Original)** The substrate of claim 23, wherein the cells further express one or more GPCRs.

25. **(Original)** A method of screening compounds and sample solutions for GPCR agonist, antagonist, inverse agonist, or desensitization active compound, comprising:

a) providing a cell expressing at least one modified arrestin, wherein the cell further comprises one or more GPCRs,

b) exposing the cell to a sample compound or compounds, wherein the sample compound or compounds may be in a sample solution,

c) detecting the modified arrestin or the GPCR along the translocation pathway, and

d) determining if the compound or compounds is a GPCR agonist, antagonist, inverse agonist, or a desensitization active compound.

26. **(Original)** The method of claim 25, wherein the arrestin or the GPCR is labeled.

27. **(Original)** The method of claim 25, wherein the GPCR is a class A, or class B receptor.

28. **(Original)** The method of claim 25, wherein the GPCR is a μ opioid, (βIAR, β2AR, or dopamine receptor.

29. **(Original)** The method of claim 25, wherein the modified arrestin or the GPCR is detected by visualization of a radioisotope, an epitope tag, an affinity label, an enzyme, a fluorescent group, or a chemiluminescent group attached to the arrestin or the GPCR.

30. **(Original)** The method of claim 25, wherein the compound is a GPCR ligand.

31. **(Original)** The method of claim 30, wherein the compound is a natural or synthetic agonist or antagonist.

32. **(Original)** A compound identified by the method of claim 25.

33. (**Original**) A method of treating a human or a non-human subject suffering from a GPCR-related disease, comprising administering to a subject in need of such treatment, an amount of the compound of claim 32 sufficient to treat the GPCR-related disease, or to lessen the symptoms thereof.

34. (**Original**) A method of treating a human or a non-human subject suffering from a GPCR-related disease, comprising administering to a subject in need of such treatement a nucleic acid encoding a modified arrestin.

35. (**Original**) The method of claim 34, wherein the nucleic acid is administered by direct injection, microprojectile bombardment, delivery via liposomes or other vesicles, or by means of a vector that can be administered by one of the foregoing methods.